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CASE REPORT

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Thanatophoric dysplasia type 1 as seen in a tertiary institution in South-East Nigeria: A case report

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Abstract*:* Thanatophoric dysplasia is a lethal form of skeletal dysplasia seen in neonates. The word 'thanatophoric' is derived from the Greek word thanatophorus meaning death bringing. Thanatophoric dysplasia results from mutations within the Fibroblast Growth Factor Receptor 3 (FGFR3) gene which is located on chromosome 4p16.3. A female neonate with dysmorphic features such as macrocephaly, frontal bossing, periorbital swelling and depressed nasal bridge was delivered to a 35year old woman. The upper and lower limbs were short with excessive skin folds. A case of female neonate with thanatophoric dysplasia is hereby reported to raise awareness of this condition and to describe the features of thanatophoric dysplasia seen in this patient .

Key words: Thanatophoric Dysplasia (TD), Fibroblast Growth Factor Receptor 3 Gene (FGFR3), dysmorphic, macrocephaly

Introduction

Thanatophoric dysplasia (TD) is a lethal form of skeletal dysplasia seen in neonates. The word 'thanatophoric is derived from the Greek word thanatophorus meaning death bringing as described by Maroteauxet al.1Thanatophoric dysplasia results from mutations within the Fibroblast Growth Factor Receptor 3 (FGFR3) gene which is located on chromosome 4p16.3.2 The condition is characterized by limb shortening, macrocephaly, folds of redundant skin, narrow chest and pulmonary hypoplasia.3,4Thanatophoric dysplasia has two major subtypes TD I and TD 2. Type 1 has a curved limb while type 2 has straight limb with cloverleaf shaped head. A case of female neonate with thanatophoric dysplasia is hereby reported to raise awareness of this condition and to describe the features of thanatophoric dysplasia seen in this patient .

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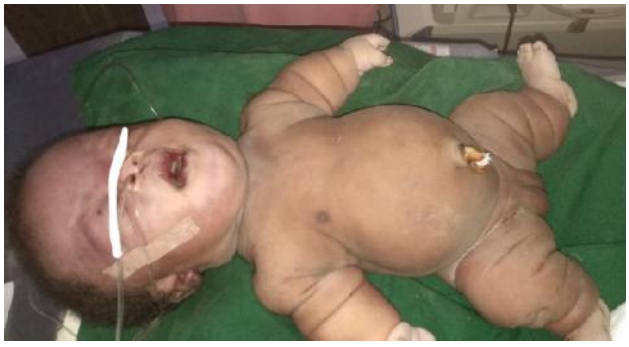
Case report

A case of a female neonate with dysmorphic features who was delivered at the Alex Ekwueme Federal University Teaching Hospital Abakaliki in May 2019 to a booked 35 year-old para 9 woman at a gestational age of 40 weeks through emergency caesarean section due to prolonged labour. Mother was not regular with antenatal visit and had taken herbal mixtures consisting of leaves mixed with alcohol at various times during the period of pregnancy. She had no history of hypertension or diabetes and no family history of congenital abnormalities. Had only one prenatal scan done during early trimester, which showed no abnormality. Father was a 60 year old man.

At delivery APGAR score was 3^{1}, $5^{5}$and 6^{10} Resuscitation with intermittent positive pressure ventilation (IPPV) with bag and mask was done at birth. She had respiratory distress and was admitted into to the newborn intensive care unit (NICU) where she was commenced on intranasal oxygen. The baby had dysmorphic features such as macrocephaly with head circumference of 41cm(>97th percentile), frontal bossing, periorbital swelling and depressed nasal bridge. The upper and lower limbs were short with excessive skin folds . The chest appeared small with protuberant abdomen. The weight was 3.25kg with a length of 38cm. diagnosis of thanatophoric dysplasia type 1 was made. The baby died 3 hours after delivery.

Newborn with features suggestive of thanatophoric dysplasia type 1



Discussion

Thanatophoric dysplasia is a lethal skeletal dysplasia and is classified in group 1 of the FGFR3 chondrodysplasia group on molecular bases.[5] It is inherited in an autosomal dominant fashion.

The prevalence of thanatophoric dysplasia has been estimated to be 1.1 per 100,000 births in Japan[6] and a prevalence of 0.21 to 0.30 per 10,000 live births in US.[7] There are no available data on the prevalence of thanatophoric dysplasia in Nigeria, this may be due to under reporting. Few case of TD has been reported in Nigeria, Joel-Medewase *et al*[8]and Komolafe*etal*[9] reported cases of TD in South-West Nigeria.

FGFR3 is a negative regulator of bone growth and its mutation is responsible for TD. The mutation results in activation of FGFR3 tyrosine kinase which sends negative signals to the chondrocytes which result in inhibition of cell division, stimulation of cell maturation and differentiation giving rise to abnormal bone development.[10] An R248C mutation has been found in the FGFR3 gene.[11] Also missense mutation of Y373c , S371C and S249C has been reported in some cases of TD.[12]

Similar features seen in this neonate like shortening of the limbs, macrocephaly, short neck, depressed nasal bridge, narrow thorax with distended abdomen has been reported by other authors.[13,14]The long bones in TD 1 are curved and appears like telephone receiver on radiographs.[15]Thanatophoric dysplasia type 2 is characterized by clover leaf shaped skull due topremature closure of coronal and lambdoid suturesand the long bones are not bent or curved. [16,17]

Most cases of TD are delivered still birth and those born alive rarely survive due to pulmonary insufficiency from narrow chest and hypoplastic lungs commonly seen in TD.[18] Thanatophoric dysplasia should be differentiated from other causes of skeletal dysplasia like achondroplasia, achondrogenesis, osteogenesis imperfecta, campomelic dysplasia. Achondroplasia is a non lethal form of chondrodysplasia characterized by big head, short limb that is marked in the proximal segment and fingers that assume trident position.[19]

TD can be diagnosed based on clinical features or use of radiographic studies either at the prenatal period by use of ultrasonography or in the immediate newborn period. On the index case the parents refused further investigation on the baby. The mother had only one prenatal ultrasound scan. A late scan in pregnancy may have detected the clinical condition and this would have prepared the parents for the birth of the baby.

An autopsy could also be done to determine the severity of the disease condition in babies with TD, autopsy was not done in this case because the parents did not give consent.

Conclusion

This is a case of a female neonate with clinical features of TD 1. The report underscores the importance of ultrasonography in pregnancy for early detection of fetal anomalies to enable appropriate counseling of the parents, preparation for birth of the baby and early intervention where indicated.

Conflict of Interest: None
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